Supplementary Materials

Intracellular Fate of the Photosensitizer Chlorin e4 with Different Carriers and Induced Metabolic Changes studied by ^{1}H NMR Spectroscopy

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Content

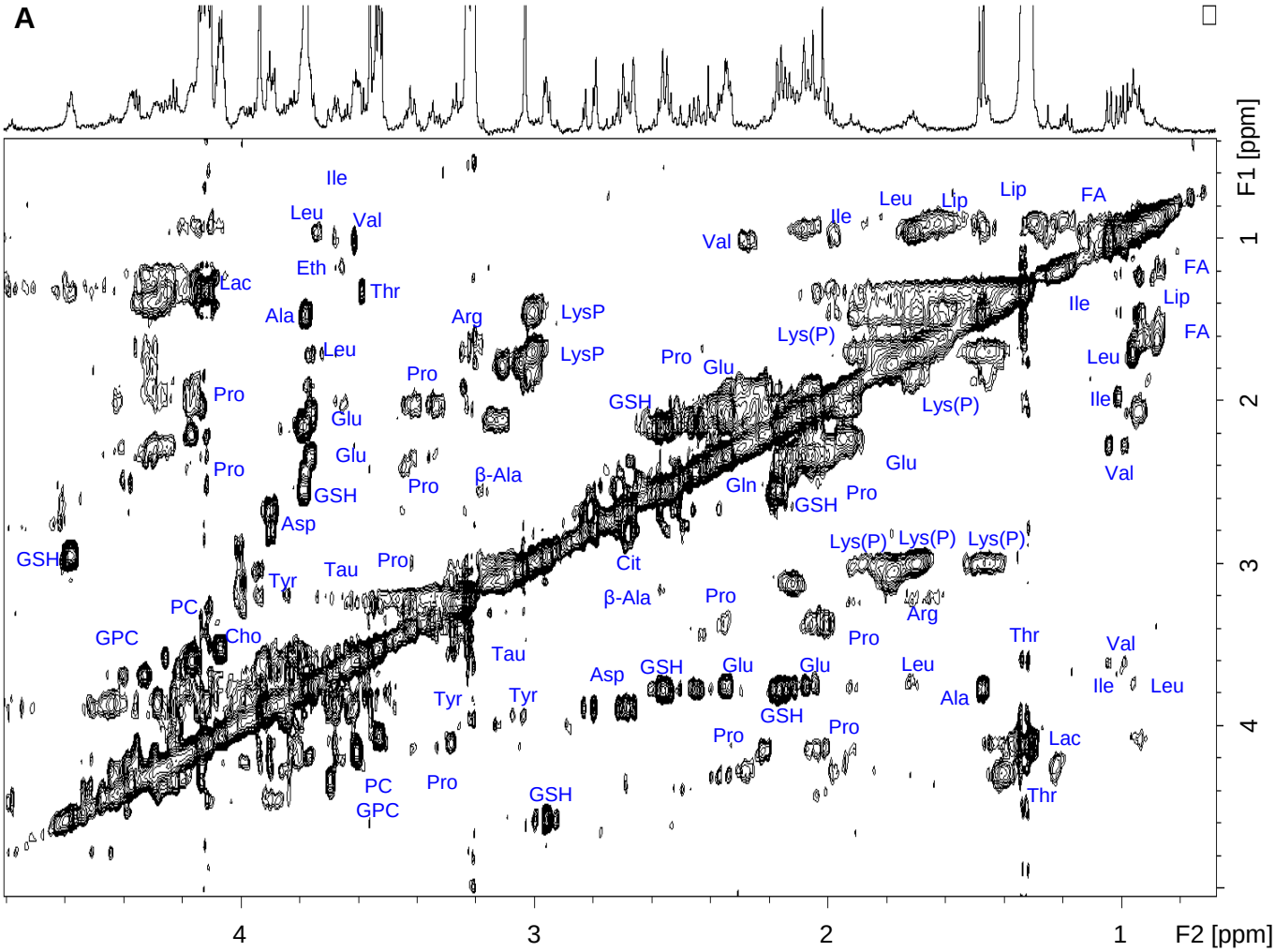


Figure S1 A: HR-MAS $^{1}H^{1}H$-TOCSY spectrum (aliphatic region) of lysed Hela cell suspension in PBS with resonance assignments (for abbreviations, see Table 2).

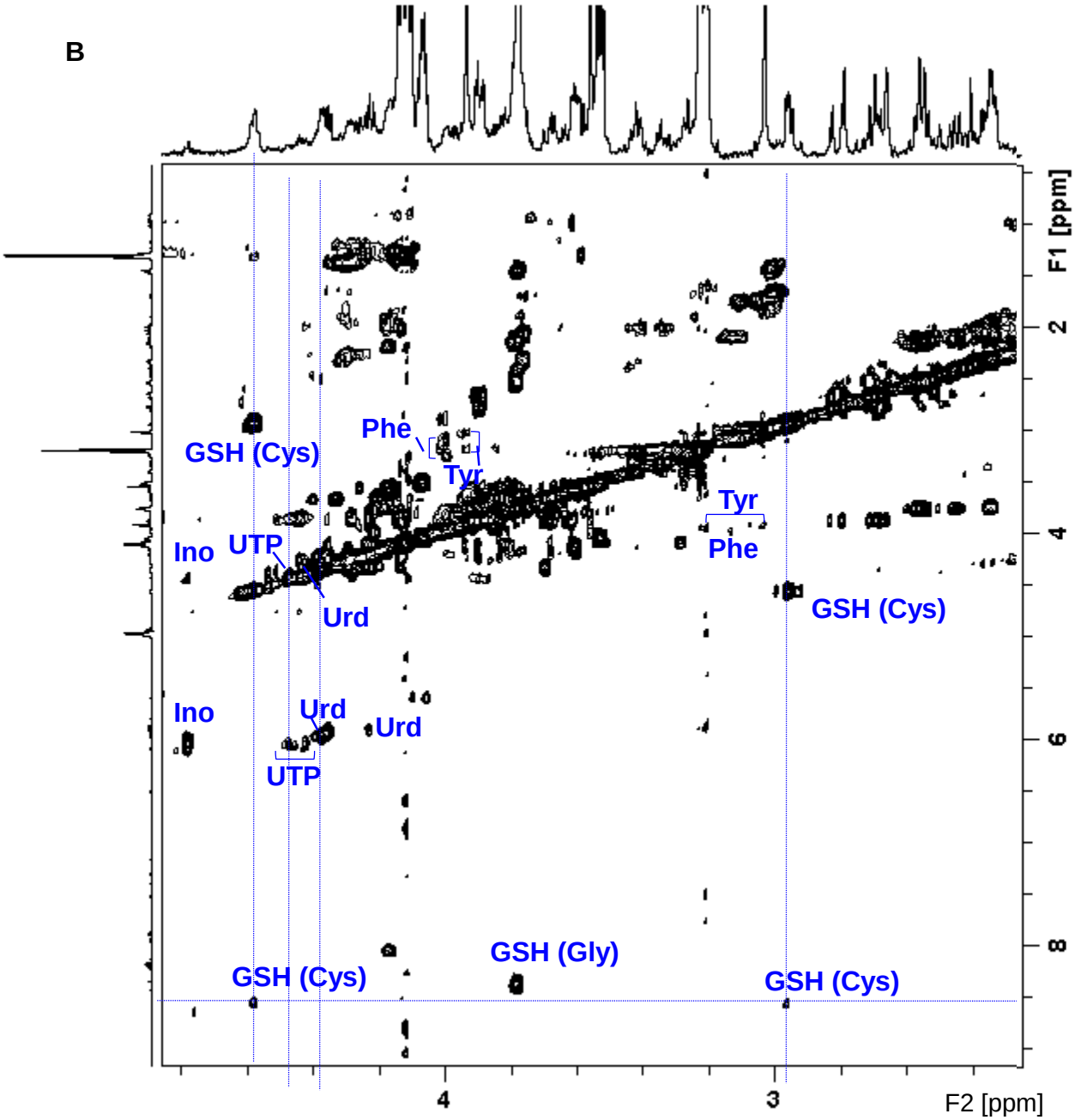


Figure S1 B: HR-MAS $^{1}H^{1}H$-TOCSY spectrum (2.2 - 4.8 ppm (F2) x 0.5 – 9 ppm (F1)) of lysed Hela cell suspension in PBS with resonance assignments (for abbreviations, see Table 2).

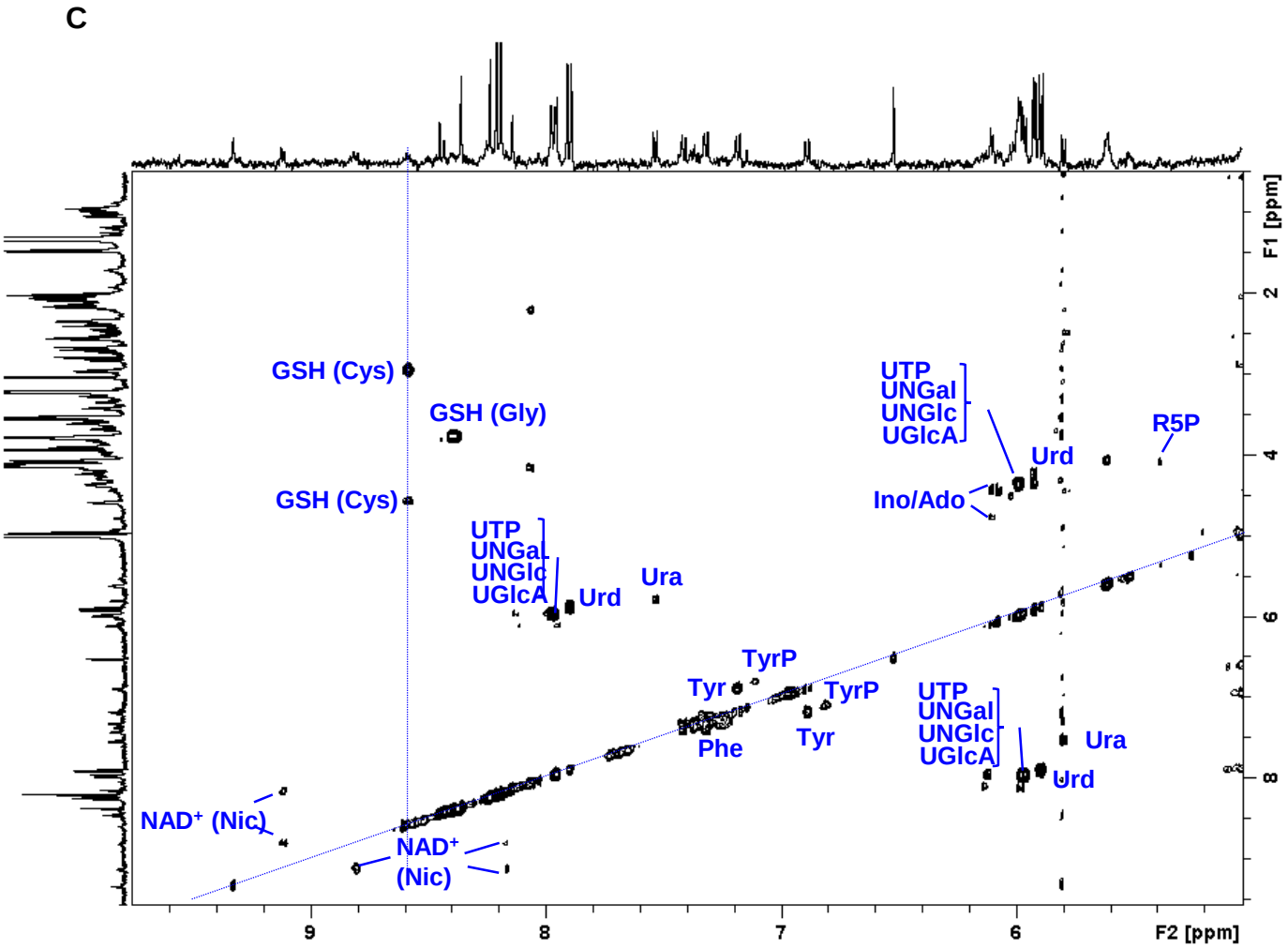


Figure S1 C: HR-MAS $^{1}H^{1}H$-TOCSY spectrum (aromatic region) of lysed Hela cell suspension in PBS with resonance assignments (for abbreviations, see Table 2).

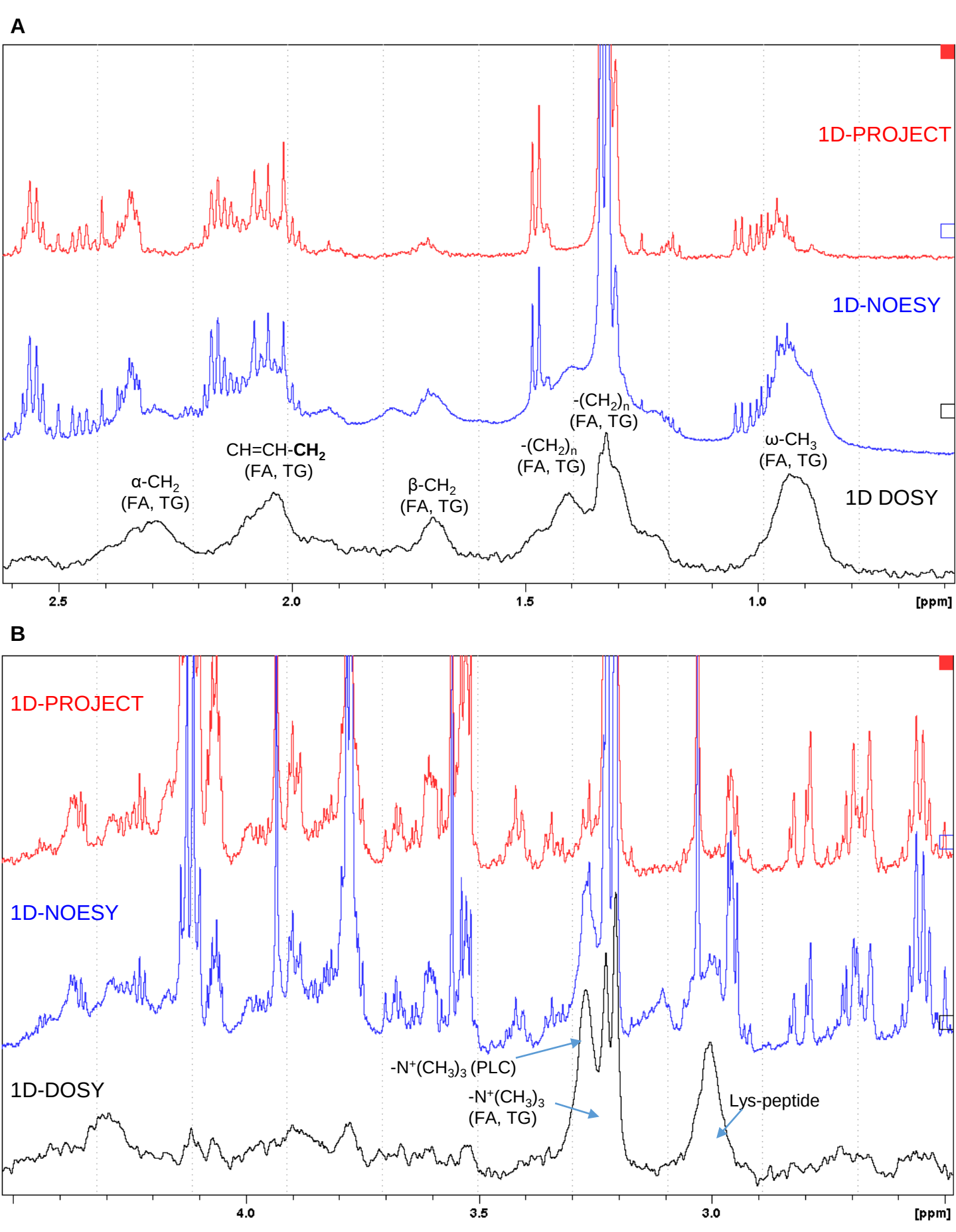
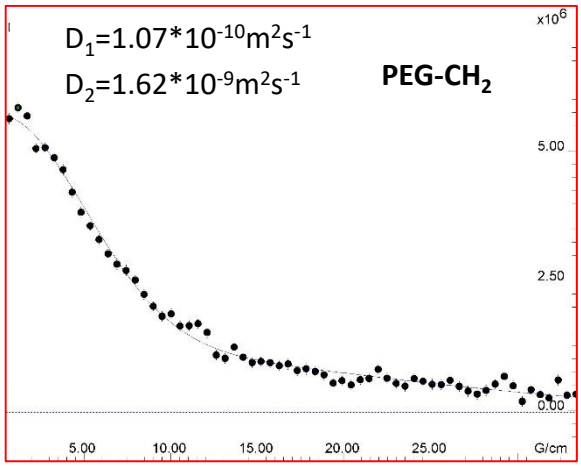
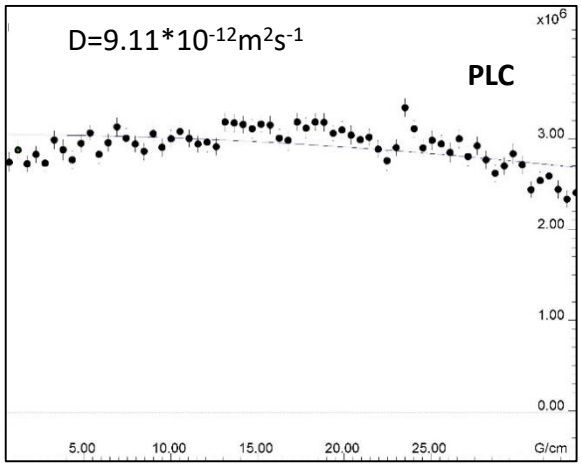
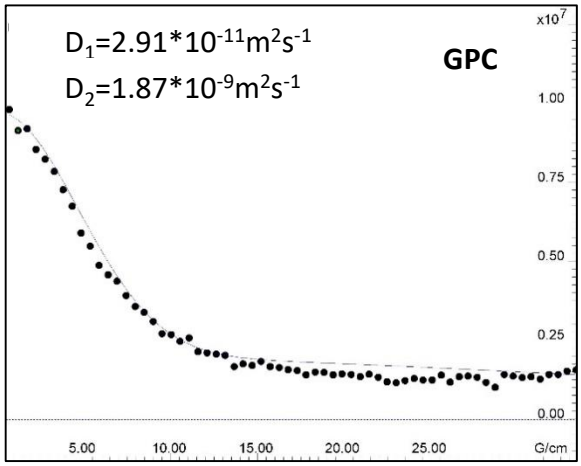
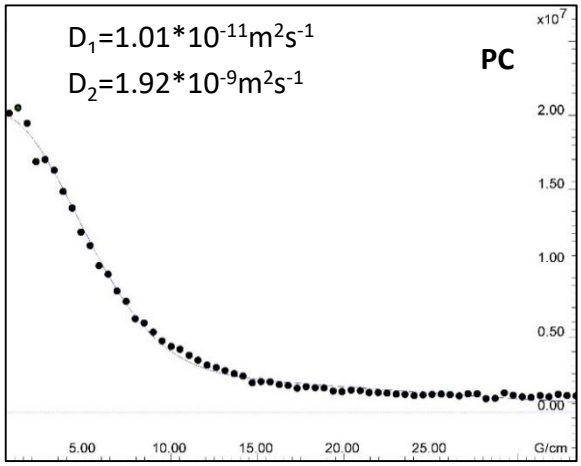


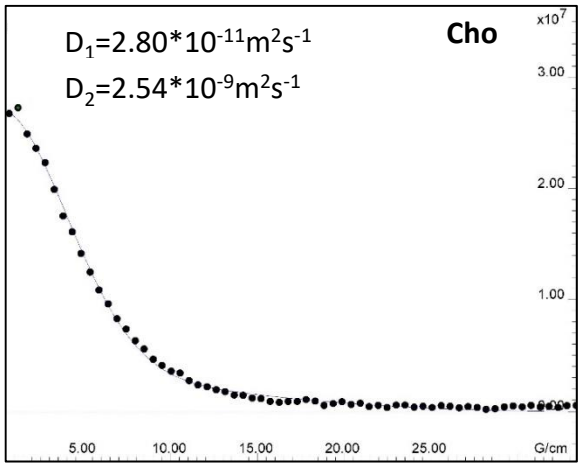
Figure S2: HR-MAS ^{1}H-1D PROJECT (red), ^{1}H-1D NOESY (blue), and ^{1}H-1D DOSY (black) spectra of lysed Hela cell suspension in PBS with resonance assignments of the 1D DOSY spectra. (**A**) Spectral region 0 – 2.6 ppm, (**B**) spectral region 2.5 – 4.5 ppm. FA: Fatty acids; TG: Tri-Glycerides; PLC: Phosphatidylcholine.











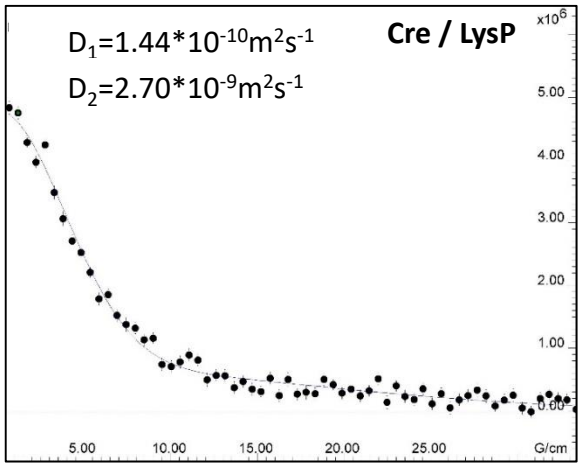


Figure S3: DOSY bi-exponential fitting curves of data plots peak intensity versus gradient strength for single peaks.

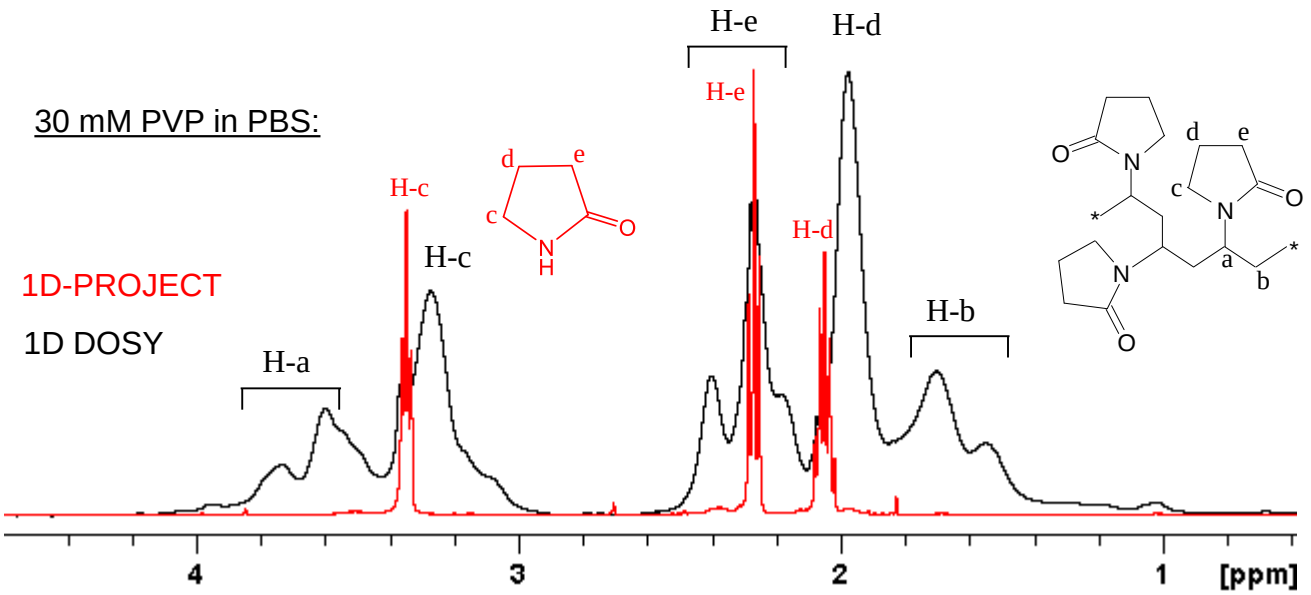


Figure S4: HR-MAS ^{1}H-T_2-edited (red) and ^{1}H-diffusion-edited (black) spectra of 30 mM PVP in PBS. The spectra demonstrate that PVP resonances are suppressed upon application of the T_2-filter applied in the cell spectra and only the resonances of the low MW impurity (pyrrolidone, red structure) remain, whereas the PVP (black structure) resonances remain visible upon application of the diffusion filter used in the cell spectra.

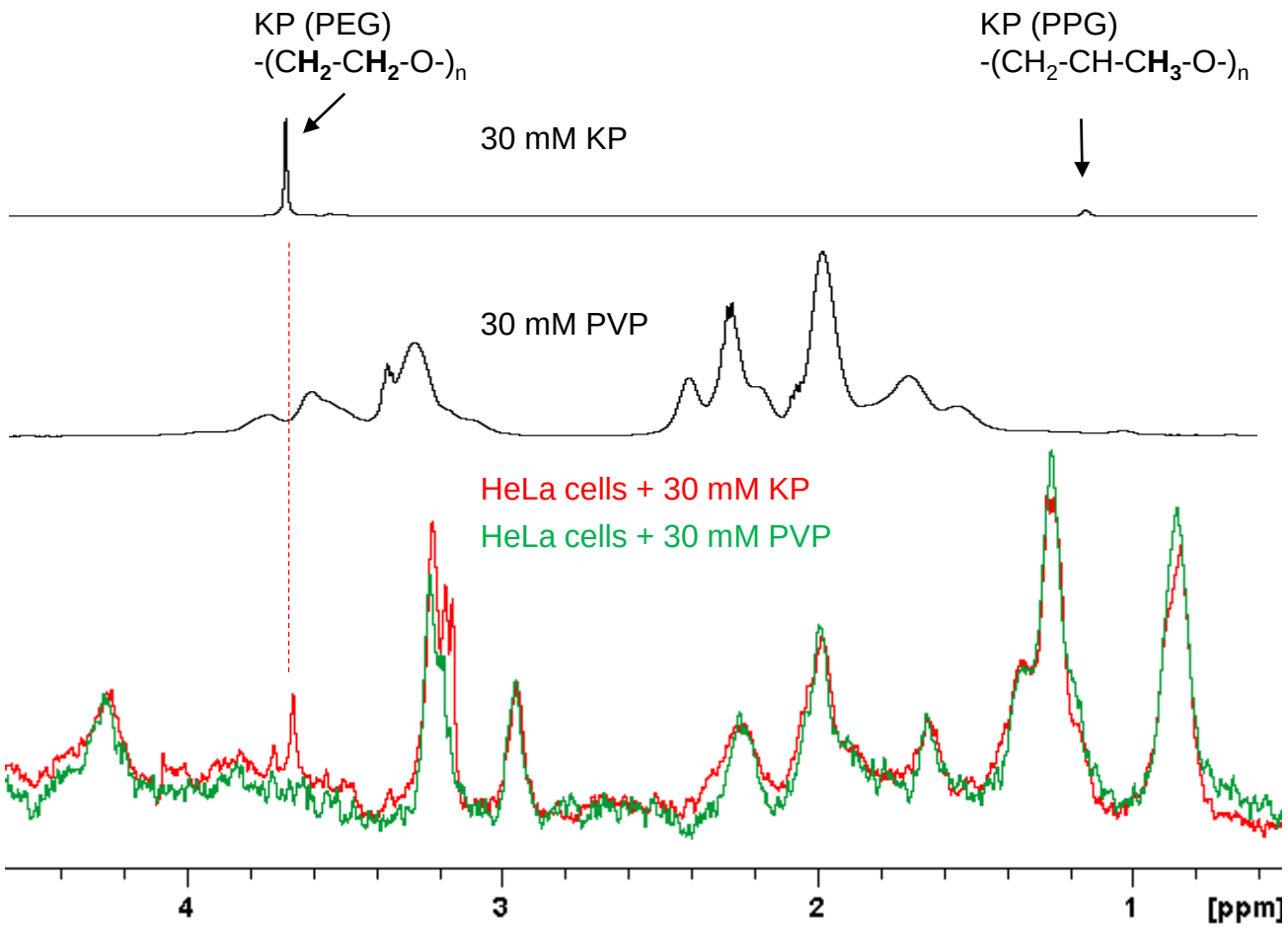


Figure S5: HR-MAS ^{1}H-diffusion-edited spectra of HeLa-cells incubated with 30 mM PVP (green), with 30 mM KP (red) and reference spectra of pure PVP and KP (30 mM in PBS, black). Whereas the KP PEG- resonance appears in the cell spectra (red line), the PVP resonances remain invisible in the cell spectra.

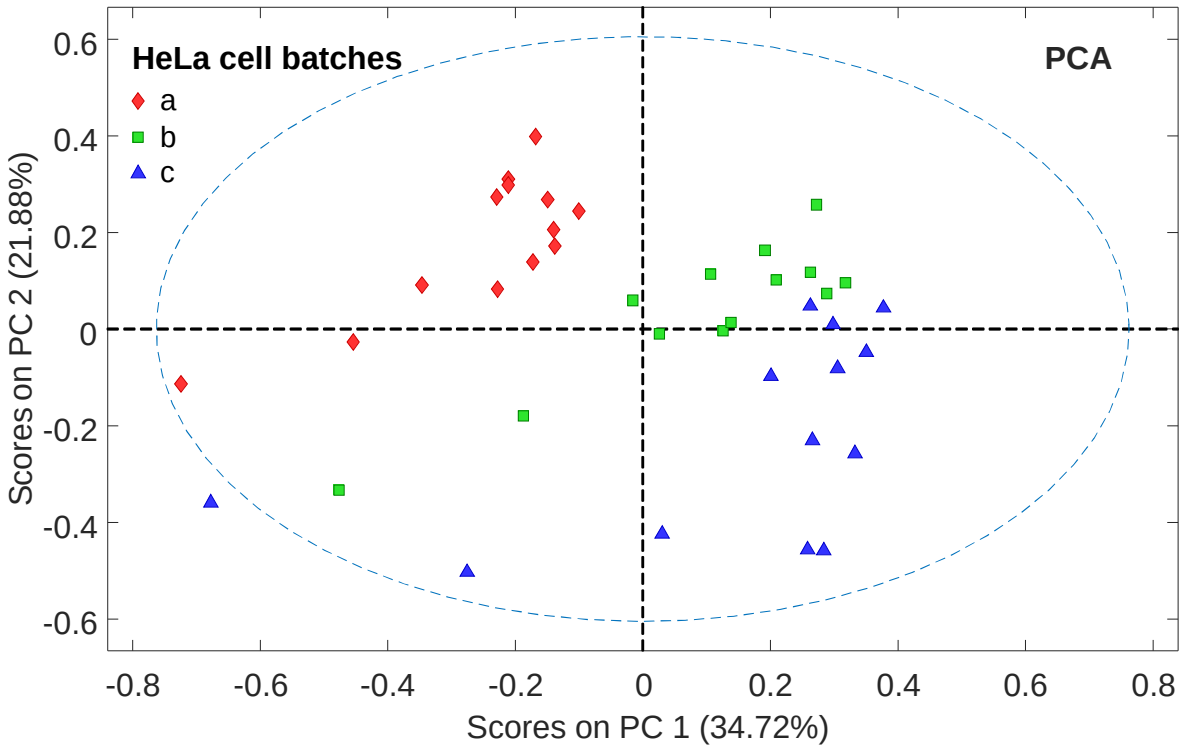


Figure S6 A: PCA scores plot displayed in Figure 6 with labelling of samples according to the three independently prepared cell batches (a, b, c). A separation of the batches is seen mainly Along PC-2. Dotted ellipsoid represents 95% confidence level.

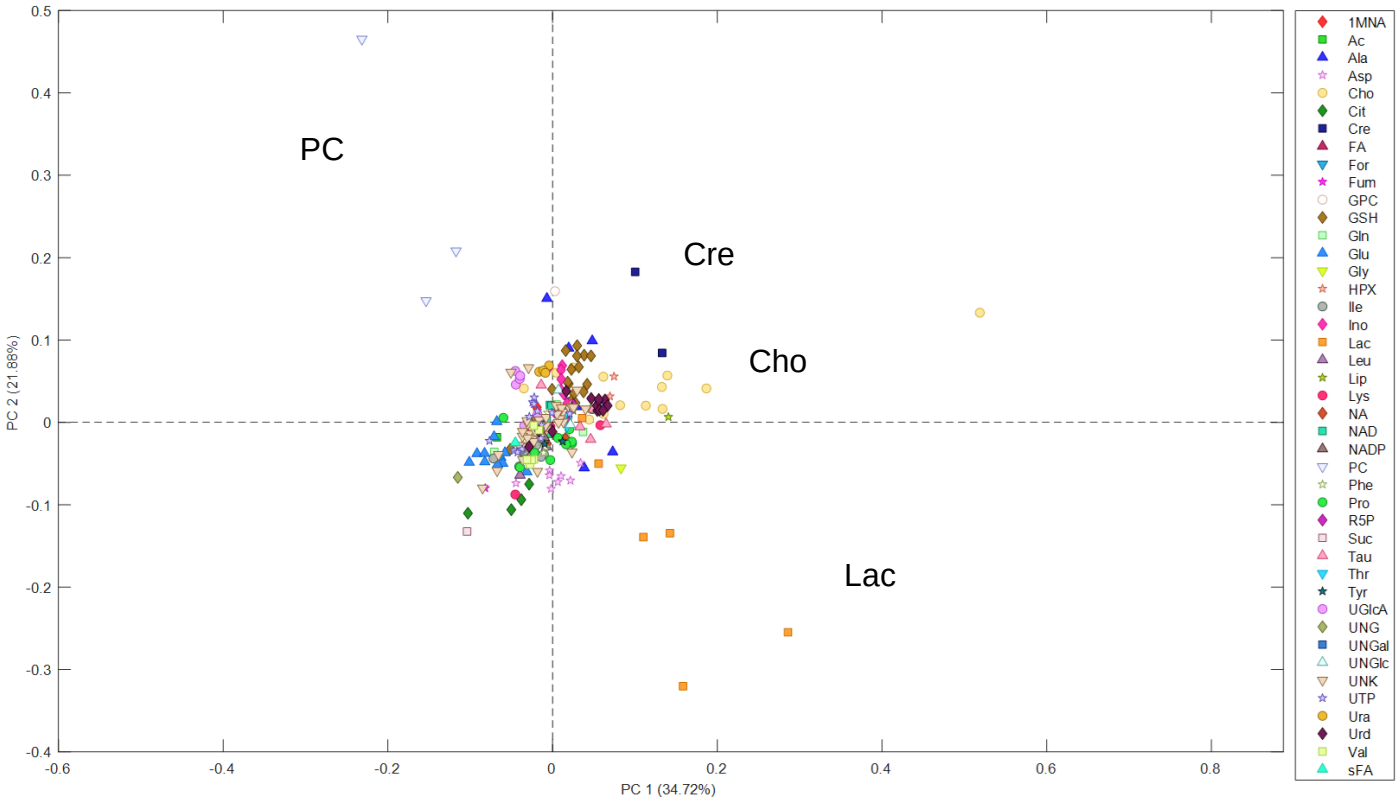


Figure S6 B: Loading plot for the principal components PC 1 and PC 2 of the scores plot displayed in Figure S6 A. Main contributors to separation of the different batches are PC and Lac.

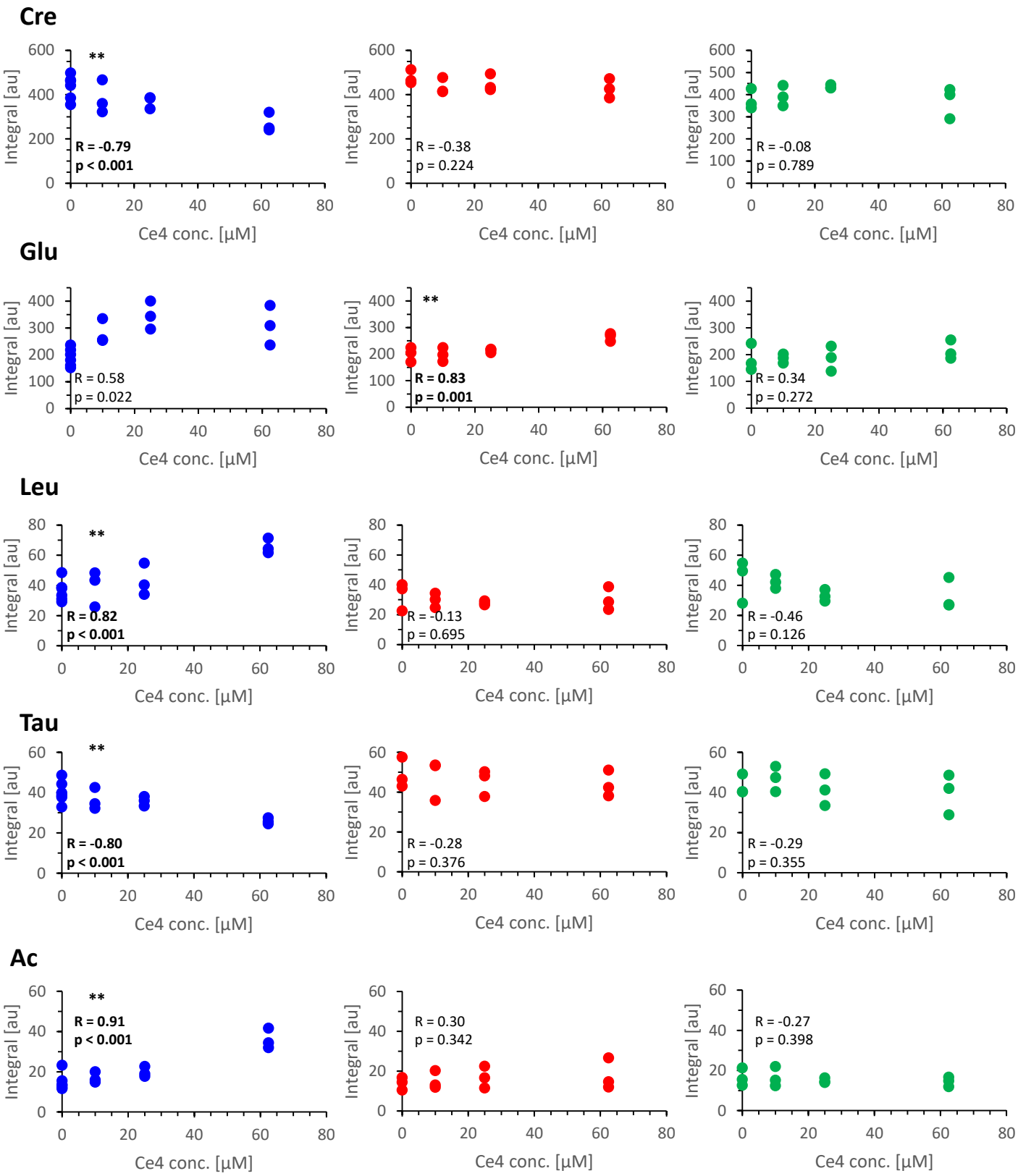


Figure S7: Plots of single metabolite integrals as function of Ce4 concentration applied without carrier (blue), with KP-micelles (red), and with PVP (green). Correlation analysis performed by fitting with resulting R-values and significance of correlation. Metabolites with highly significant ($p < 0.001$) Ce4-concentration dependent levels are marked with **.

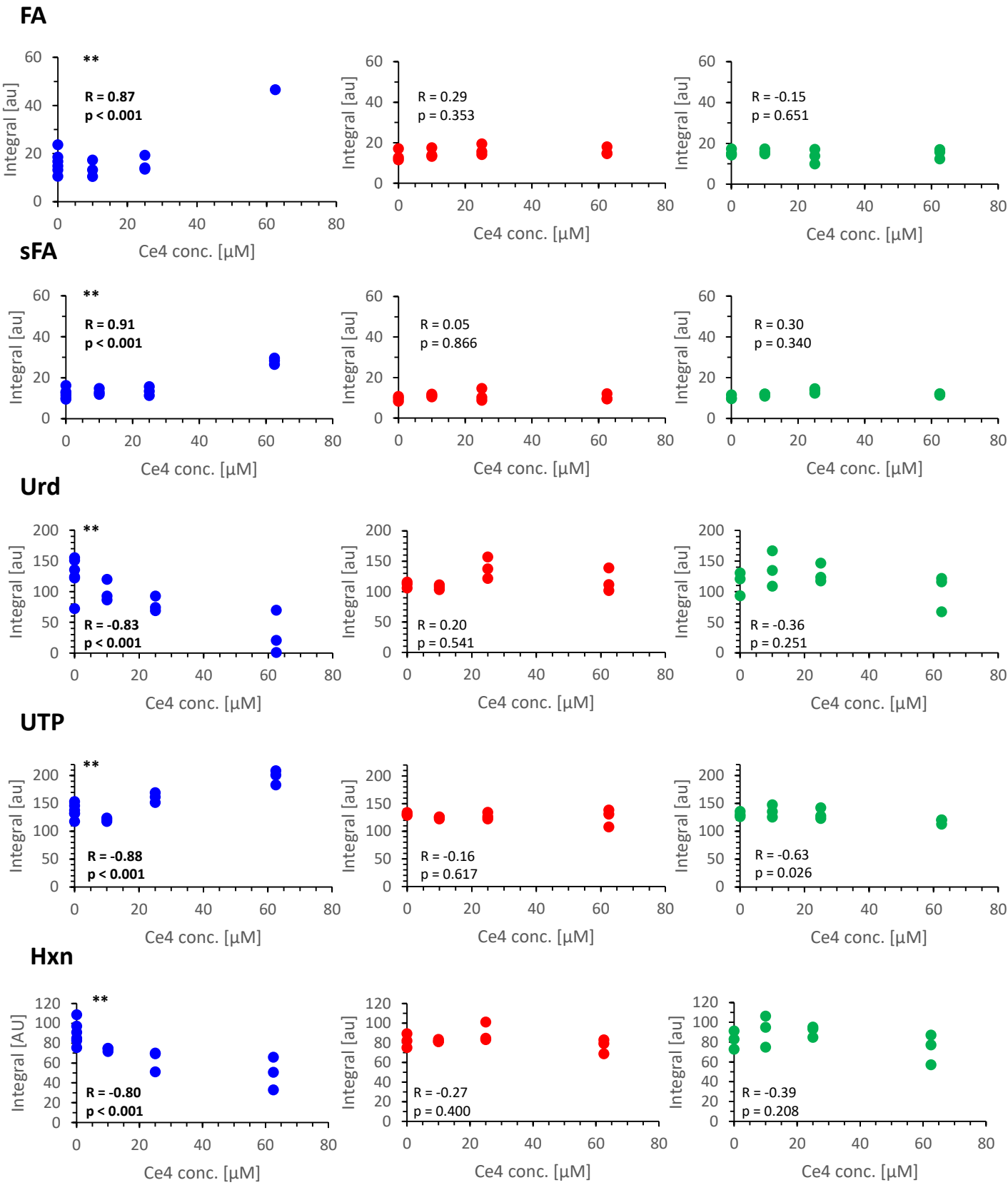


Figure S7 (continued): Plots of single metabolite integrals as function of Ce4 concentration applied without carrier (blue), with KP-micelles (red), and with PVP (green). Correlation analysis performed by fitting with resulting R-values and significance of correlation. Metabolites with highly significant ($p < 0.001$) Ce4-concentration dependent levels are marked with **.

Table S1: PLS-DA model statistics for individual sample classes, number of LVs: 2.

Model class	Classification error		R^2	
	Calculated	Cross validated	Calculated	Cross validated
Ce4-10	0.06	0.22	0.22	0.05
Ce4-25	0.097	0.07	0.19	0.06
Ce4-62.5	0	0	0.67	0.51
Ctrl 1, 2	0.17	0.40	0.19	0.09
KP	0.21	0.35	0.08	0.005
KP-Ce4-10	0.24	0.44	0.04	0
KP-Ce4-25	0.39	0.40	0.04	0.002
KP-Ce4-62.5	0.11	0.28	0.17	0.07
PVP	0.18	0.33	0.09	0.019
PVP-Ce4-10	0.21	0.54	0.06	0.002
PVP-Ce4-25	0.28	0.47	0.03	0.005
PVP-Ce4-62.5	0.15	0.32	0.09	0.018